UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JOOST VAN NEERVEN

Appeal 2007-1070
Application 09/467,901
Technology Center 1600

Decided: May 22, 2007

Before DONALD E. ADAMS, DEMETRA J. MILLS, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 1-6, 8-14, and 16-23. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF CASE

CD23 and FcεRI were known in the prior art to be the biological receptors for IgE antibody (Specification 4: 16 to 5: 15). The claimed invention relates to methods of using these known biological receptors to detect IgE antibody in a sample.

Claims 1-6 and 8-23 are pending (Br. 2). Claim 15 is stated to be allowable (Answer 2). Claims 1-6, 8-14, and 16-23 are appealed. The Examiner cites the following patents as evidence of unpatentability:

Arnold	US 6,004,745	Dec. 21, 1999
Johnson	US 6,034,066	Mar. 7, 2000
Frank	US 6,060,326	May 9, 2000
Johansen	US 6,087,188	Jul. 11, 2000

Claims 1-5, 8-14, 16, and 21-23 stand rejected under 35 U.S.C. § 103 as obvious over Johansen in view of Johnson and Frank (Answer 3).

Claims 6 and 17-20 stand rejected under 35 U.S.C. § 103 as obvious over Johansen in view of Johnson and Frank, and further in view of Arnold (Answer 7).

Within the first rejection, Claims 1-5, 8-14, 16, 21, and 22 stand or fall together; we select claim 1 as representative. However, separate arguments were provided for the patentability of claim 23;[1] thus, we consider it separately. In the second rejection, claims 6 and 17-20 stand or fall together because Appellant has not provided separate reasons for the patentability of any individual claim in this grouping; we select claim 6 as representative. *See* 37 C.F.R. § 41.37(c)(1)(vii). Claims 1, 6, and 23 read as follows:

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[1] On pages 16-18 and 25-26 of their Brief, Appellant recites the claimed features of dependent claims 2-5, 8, 9, 17-19, 20, and 21, but do not provide arguments for their patentability apart from referring to the arguments set forth for independent claims 1 and 6. "A statement which merely points out what a claim recites will not be considered an argument for separate patentability of the claim." 37 C.F.R. § 41.37(c)(1)(vii).

1. A method of detecting and/or quantifying an IgE antibody specific to a ligand in the form of an antigen, an antibody, or a hapten in a liquid sample suspected to contain the IgE antibody comprising the steps of:

(a) contacting (i) the sample with (ii) a free dissolved ligand in the form of an antigen, an antibody, or a hapten to form a mixture I comprising complexes that comprise the IgE antibody and the ligand (IgE-containing complexes),

(b) mixing the mixture I with a carrier to which is bound (iii) an IgE receptor, wherein said IgE receptor is CD23 (FcεRII) and/or FcεRI, to form a mixture II comprising carrier-bound IgE-containing complexes,

(c) separating the carrier-bound IgE-containing complexes from the mixture II, and

(d) determining the amount of the carrier-bound IgE-containing complexes formed by detecting a label present in the carrier-bound IgE-containing complexes,

wherein the label to be detected is associated with the ligand or the IgE antibody and wherein the label to be detected is added to the complexes present in steps (a), (b), or (c) and does not form part of the carrier.

6. A method of detecting and/or quantifying an IgE antibody specific to a ligand in the form of an antigen, an antibody, or a hapten in a liquid sample suspected to contain the IgE antibody comprising the steps of:

(a) contacting (i) the sample with (ii) a free dissolved ligand in the form of an antigen, an antibody, or a hapten to form a mixture I comprising complexes that comprise the IgE antibody and the ligand (IgE-containing complexes),

(b) mixing the mixture I with a carrier to which is bound (iii) an IgE receptor, wherein said IgE receptor is CD23 (FcεRII) and/or FcεRI, to form a mixture II comprising carrier-bound IgE-containing complexes,

(c) separating the carrier-bound IgE-containing complexes from the mixture II,

(d) adding a label compound to the carrier-bound IgE-containing complexes resulting from the separation step (c) to form a mixture II',

(e) separating the labeled carrier-bound IgE-containing complexes from the mixture II', and

(f) determining the amount of the carrier-bound IgE-containing complexes formed by detecting the label present in the carrier-bound IgE-containing complexes,

wherein the label compound is associated with the ligand or the IgE antibody.

23. A method of detecting and/or quantifying physiologically active forms of an IgE antibody specific to a ligand in the form of an antigen, an antibody, or a hapten in liquid sample suspected to contain the IgE antibody by simulating *in vivo* interactions between the IgE antibody, the IgE antibody's ligand and the IgE antibody's receptor, comprising the steps of:

(a) contacting (i) the sample with (ii) a free dissolved ligand in the form of an antigen, an antibody, or a hapten to form a mixture I comprising complexes that comprise the IgE antibody and the ligand (IgE-containing complexes),

(b) mixing the mixture I with a carrier to which is bound (iii) an IgE receptor, wherein said IgE receptor is CD23 (FcεRII) and/or FcεRI, to form a mixture II comprising carrier-bound IgE-containing complexes, and wherein the complexes that comprise the IgE antibody and the ligand are formed prior

to contact with the IgE receptor to simulate *in vivo* interactions between the IgE antibody, the ligand, and the IgE receptor,

(c) separating the carrier-bound IgE-containing complexes from the mixture II, and

(d) detecting and/or quantifying physiologically active forms of ligand-specific IgE bound to said receptor by determining the amount of the carrier-bound IgE-containing complexes formed by detecting a label present in the carrier-bound IgE-containing complexes,

wherein the label to be detected is associated with the ligand or the IgE antibody and wherein the label to be detected is added to the complexes present in steps (a), (b), or (c) and does not form part of the carrier and wherein *in vivo* interactions between the IgE antibody, the IgE antibody's ligand and the IgE antibody's receptor are simulated to measure physiologically active forms of IgE.

FINDINGS OF ACT

Johansen

1. Johansen describes an IgE assay which is specific for an IgE antibody; the IgE antibody recognizes a specific antigen or hapten of interest (Johansen, col. 4, ll. 50-62 and col. 5, ll. 50-60; Answer 4).

2. The assay contains: 1) specific IgE-antibody; 2) a specific allergen (antigen or hapten) bound to biotin; 3) a monoclonal mouse anti-IgE bound to magnetic particles; and 4) a chemiluminescent avidin-acridinium ester label (Johansen, col. 5, ll. 50-60; Answer 4).

3. The specific IgE-antibody (present in a "sample") is mixed with the specific allergen bound to biotin ("ligand antigen") and the anti-IgE bound

to magnetic particles ("antibody directed against the [IgE] antibody") to form a first complex (Johansen, col. 3, ll. 37-42; col. 5, ll. 50-60; Answer 4).

4. The label ("chemiluminescent acridinium compound") is added to the first complex to form a second complex (Johansen, col. 3, ll. 43-46; Answer 4).

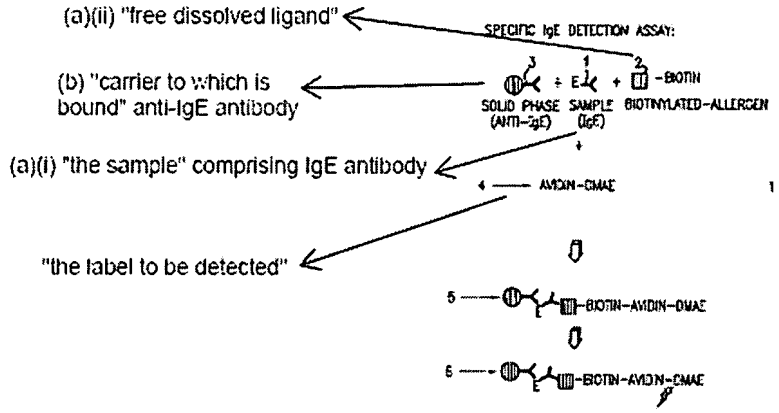
5. The second complex is separated from the liquid phase and the label is detected (Johansen, col. 3, ll. 47-51; Answer 4).

6. Example 2 describes detection and quantification of a specific IgE according to this method (Johansen, cols. 8-9).

7. Johansen's Fig. 1 illustrates the assay steps.

8. The correspondence between the steps recited in instant claim 1 and Johansen's specific IgE assay is shown below.

Claim 1 Johansen's Fig. 1



9. Johansen's assay meets the limitations of steps (a)-(d) of claim 1, but does not describe using an IgE receptor which is "CD23 (FcεRII) and/or FcεR1" as recited in step (b). (Answer 5).

Frank

10. Frank describes "a method to detect canine IgE using a canine Fc epsilon receptor ($Fc_{\varepsilon}R$) to detect canine IgE antibodies in a biological sample from a canid" (Frank, Abstract).

11. Frank states:

> The present invention relates to the discovery that purified high affinity canine Fc epsilon receptor (i.e., $Fc_{\varepsilon}RI$; referred to herein as $Fc_{\varepsilon}R$) can be used in canine epsilon immunoglobulin (referred to herein as IgE or IgE antibody)-based detection (e.g., diagnostic, screening) methods and kits.

(Frank, col. 2, ll. 13-17.)

12. Frank describes the advantage of using $Fc_{\varepsilon}R$ in an IgE detection assay instead of anti-IgE.

> [A]ntibodies that bind selectively to . . . (i.e., anti-IgE antibodies) . . . have been used to detect IgE. These anti-IgE antibodies, however, can cross-react with other antibody idiotypes . . . . The discovery of the present invention includes the use of . . . ($Fc_{\varepsilon}R$) . . . to detect the presence of IgE in a putative IgE-containing composition. . . . A canine $Fc_{\varepsilon}R$ molecule provides an advantage over, for example anti-IgE antibodies, to detect IgE because a canine $Fc_{\varepsilon}R$ molecule . . . can bind to a canine IgE with more specificity . . . and more sensitivity . . . than anti-IgE binding antibodies.

(Frank, col. 1, ll. 24-41.)

13.

> The use of canine $Fc_{\varepsilon}R$ in diagnostic methods and kits is unexpected because the use of canine $Fc_{\varepsilon}R$ avoids complications presented by use of antibodies that bind to IgE (i.e., anti-IgE antibodies). Such complications include, for example, non-specific binding of anti-IgE antibodies to other classes of immunoglobulin such as gamma immunoglobulin (i.e., IgG).

(Frank, col. 2, ll. 17-25.)

Johnson

14. Johnson teaches that CD23 is a cellular receptor for IgE (Answer 6).

Obviousness over Johansen and Frank in view of Johnson

15. The Examiner contends:

> It would have been obvious to one of ordinary skill in the art to use the IgE receptors of Johnson et al. and Frank et al. to measure IgE according to the method of Johansen et al. since both of these receptors, CD23 and [FcεR], are specific to IgE antibody and because [FcεR] and CD23 can bind to IgE with less isotype cross-reactivity and more sensitivity than anti-IgE binding antibodies. (See Frank et al. Col. 1, lines 19-34).

(Answer 6.)

Arnold

16. Arnold teaches

> in the background section that a typical sandwich assay involve[s] incubating an immobilized antibody (IgE receptor) with a test medium (sample). Antigens, if in the medium, will bind to the antibody. After incubation, unbound antigen is removed in a separation step. After a second, or simultaneous incubation with a solution of labeled antibody, the bound antigen becomes sandwiched between the immobilized antibody and the labeled antibody. After a second separation step, the amount of labeled antibody can be determined as a measure of the antigen in the medium. (see col. 1, lines 55-66).

(Answer 7.)

Obviousness over Arnold

17. The Examiner states that it would have been obvious to a person of ordinary skill in the art to have utilized first and second separation steps as taught by Arnold for their known advantages (Answer 7).

DISCUSSION

Obviousness of claims 1-5, 8-14, 16, and 21-23

Claims 1-5, 8-14, 16, and 21-23 stand rejected under 35 U.S.C. § 103 as obvious over Johansen in view of Johnson and Frank (Answer 3).

A claimed invention is obvious "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). To make this determination, we consider in the context of the knowledge and level of skill possessed by a person of ordinary skill in the art whether such a person would have had reason to combine the prior art in the fashion claimed by the application at issue. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 82 USPQ2d 1385, 1396 (2007).

In this case, we find that the Examiner has presented sufficient evidence that a person of ordinary skill in the art would have had adequate reason at the time the application was filed to have utilized Frank's FcεR molecule in Johansen's method of detecting specific IgE antibodies. Frank explicitly states that its FcεR molecule is an improvement over anti-IgE antibody (i.e., the anti-IgE antibody utilized in Johansen's method) "because the use of canine $Fc_{\varepsilon}R$ avoids complications presented by the use of . . . anti-IgE (i.e., anti-IgE antibodies)," such as non-specific binding (Frank, col. 2, ll. 19-21; FF 12-13). Frank recognizes that this property is advantageous in IgE antibody-based detection (e.g., diagnostic, screening) methods and kits (Frank, col. 2, ll. 14-17; FF 11). The skilled worker would recognize this as

suggestion to utilize $Fc_{\varepsilon}R$ for IgE detection, including in methods such as the one described by Johansen.

Appellant contends that "a general suggestion that an IgE receptor might be used in the genus of detection assays does not suggest its use in the particular method of the invention" (Br. 14). We do not agree. Precise teachings directed to the specific subject matter of a claim are not required to reach a conclusion of obviousness. *KSR*, 82 USPQ2d at 1396. "[T]he teaching, motivation, or suggestion may be implicit from the prior art as a whole, rather than expressly stated in the references. . . . The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kahn*, 441 F.3d 977, 987-988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). In this case, Frank expressly teaches problems associated with anti-IgE antibodies – the same antibodies used by Johansen – and suggests a solution: substituting FcεR because it more specific and sensitive, providing "an advantage over . . . anti-IgE antibodies . . . to detect IgE" (Frank, col. 1, ll. 36-38; FF 13).

Appellant also argues that "skilled [worker] would be encouraged to use Frank's . . . method in its entirety" which involves the use of not only FcεR but also anti-IgE (Br. 13). Appellant asserts that Frank "describes using FcεR with antibodies, not substituting antibodies for receptors" (Br. 13). We do not find this argument persuasive. The disclosure that Appellant is apparently referring to is Frank's teaching that anti-IgE antibodies can be used to detect the FcεR molecule: IgE complex (Frank, col. 9, ll. 57-60).

However, Frank teaches different methods of detecting IgE using different types of labeling reagents (col. 8, l. 50 to col. 9, l. 60), only one embodiment which uses anti-IgE antibodies. In contrast, all Frank's embodiments utilize FcεR to detect IgE. FcεR as a detection reagent is characterized by Frank as its "discovery" (Frank, col. 2, ll. 13-15; FF 11-13). This discovery is not masked or denigrated by Frank's teaching that FcεR can be used in different assay formats (Br. 15-16), including formats which combine it with an anti-IgE antibody. To the contrary, these teachings show the suitability of FcεR in a wide range IgE detection methods, providing the reason to have combined Frank's disclosure with Johansen.

We also agree with the Examiner that Frank's teaching that FcεR can be used to detect IgE antibodies in a sample would have led a person of ordinary skill in the art to reasonably expect that FcεR could be used successfully in Johansen's IgE detection method (Answer 9). Appellant argues that the Examiner has not satisfied the initial burden of showing a reasonable expectation of success (Br. 16), but has not explained why Frank's disclosure that FcεR works to detect IgE in a biological sample is insufficient evidence to meet this burden.

Claim 23

It is stated by Appellant, especially with respect to claim 23 (Br. 19), that

> Prior systems that use, for example, anti-IgE antibodies to bind to the IgE antibodies are artificial and useful for simply measuring the concentration of specific immunoglobulins in a sample. In fact, it can be said that prior systems are artificial because they measure the total concentration of immunoglobulin in a sample. See specification at page 1, lines

> 9-29. In contrast, however, by using IgE receptors, the invention focuses on those antibodies that are biologically active, thus measuring the relevant *in vivo* level of IgE. See specification at page 6, lines 1-6.

(Br. 5-6). Claim 23 expressly recites that "in vivo interactions . . . are simulated" in its method.

While the claimed method may facilitate the measurement of levels of IgE "that are most likely to be active *in vivo*" (Br. 7), the method itself is suggested by the prior art and these properties are inherent to carrying it out. "Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." *In re Baxter Travenol Labs.*, 952 F.2d 388, 392, 21 USPQ2d 1281, 1285 (Fed. Cir. 1991).

Johnson

The IgE receptor in claim 1 is "CD23 (FcεRII) and/or FcεRI"; thus, the receptor can be one of three different embodiments: 1) CD23 alone, 2) FcεRI, or 3) CD23 and FcεRI. Since we have concluded that the combination of Johansen in view of Frank suggests the use of FcεRI in the claimed assay, it is unnecessary for us to consider the other embodiments which involve CD23. A claim covering a plurality of embodiments is unpatentable under § 103 if the prior art demonstrates the obviousness of any one of them. *In re Klein*, 987 F.2d 1569, 1570, 26 USPQ2d 1133, 1134 (Fed. Cir. 1993). For this reason, we do not address Appellant's arguments regarding Johnson which was cited for its teaching of CD23.

Conclusion

For the foregoing reasons, we affirm the rejection of claim 1 as obvious over Johansen in view of Johnson and Frank (Answer 3). Claims 2-5, 8-14, 16, and 21-23 fall with claim 1 because separate arguments for their patentability were not provided.

Obviousness of claims 6 and 17-20

Claims 6 and 17-20 stand rejected under 35 U.S.C. § 103 as obvious over Johansen in view of Johnson and Frank, and further in view of Arnold (Answer 7).

Claim 6 further requires adding a label after a first separation step followed by a second separation step to separate non-complexed label from the labeled complex (Br. 21; Answer 7).

The Examiner has provided evidence that a person of ordinary skill in the art would have reason to have combined Arnold with Johansen and Frank for Arnold's known advantages (Answer 7; FF 17).

Appellant argues that Arnold does not "cure" the "defect" in the combination of Johansen and Frank (Br. 22). They also argue that Arnold's assay differs from the claimed assay in teaching immobilized capture antibody (Br. 22).

> [T]hus the interaction between the antibody and the ligand does not take place freely in solution . . . [as required by claim 6]. There is no teaching in Arnold suggesting that such an assay could be adapted to detect antibodies let alone using an antibody receptor that is not immobilized to do it.

(Br. 22.)

We concur with the Examiner's finding that Arnold teaches that two-step antibody separation methods are conventional in the art. Arnold states that the label can be added in either a second step or "simultaneous" with the first incubation step with antibody and antigen (Arnold, col. 1, l. 60; FF 16), indicating the interchangeability of a one-step method (e.g., Johansen) with a two-step method (e.g., Arnold). Appellant's arguments address the suitability of Arnold's particular assay method when combined with Johansen and Frank, not the use of the two-step assay format described in Arnold's background. Consequently, we do not find Appellant to have rebutted the prima facie case of obviousness.

Conclusion

The rejection of claim 6 is affirmed. Claims 17-20 fall with claim 6 because different arguments for their patentability were not provided.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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